Lekshmi Dharmarajan

Curriculum Vitae

Education

2015-present	**Ph.D. in computational biology**, *Dept. of Biosystems Science and Engineering*, ETH-Zürich, Switzerland.
2012-2014	**Masters of Science in Biotechnology (Major in Systems Biology)**, *ETH Zürich*, Switzerland, *GPA − 5.52/6.00*.
2008-2012	**B.Tech. Industrial Biotechnology**, *SASTRA University*, India, *GPA − 9.05/10*.

Ph.D. Thesis

Title
Analyzing single-cell longitudinal data with nonlinear mixed effect models

Supervisors
Prof. Dr. Joerg Stelling

Description
I defended my PhD thesis in May 2020, and expect the final confirmation in September, 2020. During the course of my PhD, I have designed and executed computational projects and also ventured into the wet-lab to generate my own microscopy images using budding yeast. I implemented a computational pipeline to infer nonlinear mixed effect models (NLMEs) of signaling networks from time-lapse imaging data. Using the model we inferred with the pipeline, we identified which processes in endocytosis contribute most to the observed heterogeneity in a population of single-cells. My pet project involves modeling the impact of mutations found in cancer on MAPK signaling dynamics. My main expertise lies in longitudinal data analysis, modeling biological data with mechanistic models, nonlinear optimization and uncertainty quantification. In addition, I have framed exercises and organized tutorials for a semester course on Experimental Design for master students of Biotechnology at ETH.

Research Experience

Oct 2014 - May 2015
Research Trainee, under *Dr. Julio Saez-Roderiguez*, Systems Biomedicine Group, European Bioinformatics Institute, Hinxton, UK (currently at University of Heidelberg).
Research assistant, assisting in projects
- ⋆ Developed a pipeline to analyze micro-array data and SNPs arrays: used meta-analysis to combine two different studies, and applied regularized regression methods to understand heterogeneity in Multiple Sclerosis patients using gene expression data from PBMCs and SNPs in R.
- ⋆ Optimized existing code and identified causal edges in a gene network using Integer Linear Programming with CPLEX interfaced with Python.

Nov 2013 - Jul 2014
Master Thesis, under *Prof. Dr. Niko Beerenwinkel*, Computational Biology group, ETH-Zürich.
Inferring Pathways in Glioblastoma and Identifying Hidden Nodes in Networks using Nested Effect Models.
- ⋆ Extended a probabilistic graphical framework called 'nested effect models' to account for multiple perturbations to a gene in R, interfaced with C.
- ⋆ Used the extension and inferred network structures of pathways with most altered genes in Glioblastoma, using publicly available data sets.

Aug 2013 - Nov 2013
Research Project, under *Dr. Moritz Lang* and *Prof. Dr. Joerg Stelling*, Computational Biology group, ETH-Zürich.
In-silico analysis of a bistable switch in *Saccharomyces cerevisiae*
- ⋆ Described a synthetic biological switch using an ODE based model in MATLAB.
- ⋆ Calibrated the model from data, predicted regimes of the model parameters showing bistability, and assessed the impact of noise on the system.

Dec 2011 - Apr 2012
Bachelor Thesis, under *Prof. Dr. Amol Kulkarni, Industrial Flow Modeling Group*, National Chemical Laboratories, Pune.
Studied the effect of mechanical vibrations in stagnant liquids and flow in microchannels.
- ⋆ Modeled the phenomenon in MATLAB to explain our observations.

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Publications

Journal Paper | *Gnügge, R.,* **Dharmarajan, L.**, *Lang, M. and Stelling, J., 2016. An Orthogonal Permease-Inducer-Repressor Feedback Loop Shows Bistability.* **ACS synthetic biology**, *5(10), pp.1098-1107.*

Journal Paper | **Dharmarajan, L.***, *Kaltenbach, H. M.*, Rudolf, F., and Stelling, J. (2019). A simple and flexible computational framework for inferring sources of heterogeneity from single-cell dynamics.* **Cell systems**, *8(1), 15-26.*

Oral Presentations

Nov 2018 | ***"Inference of nonlinear mixed effect models from single-cell time-lapse data using two-stage approaches"***, *Intra-departmental seminar, ETH-Zürich, Switzerland*

Sep 2019 | ***"A simple and flexible computational framework for inferring sources of heterogeneity from single-cell dynamics."***, *[BC]2 conference BASEL LIFE, Switzerland.* **Won the best flash talk prize.**

Poster Presentations

Jul 2015 | *Classifying and Understanding Heterogeneous Prognosis of Multiple Sclerosis in Patients*, at International Conference on Systems Biology of Human Disease, Heidelberg, Germany

Nov 2017 | *Inference of nonlinear mixed effect models from single-cell data using two-stage approaches*, SystemsX Conference, Switzerland

Mar 2018 | *Inference of nonlinear mixed effect models from single-cell time-lapse data using two-stage approaches*, Single-Cell Biology Conference, United Kingdom

September 2019 | *Simple and flexible framework to infer sources of cell-to-cell variation in time-lapse imaging data*, [BC]2 conference BASEL LIFE, Switzerland

Mentoring experience

2017 and 2018 | *Teaching Assistant for Design of Experiments (636-0022-00L) course at ETH-Zurich*: Designed exercises and helped establish a new course covering concepts of randomization, replication, factorial and fractional factorial designs, confounding and response surface models.

Jun-Dec 2016 | *Supervised master thesis* of Charlie Pieterman: In-silico study of the impact of mutation order in MAPK pathway

Sep-Nov 2018 | *Supervised research project* of Anna Bailach: Comparison of parameter estimation of ODE models from single-cell and averaged data.

Jan-Jun 2019 | *Supervised master thesis of Li Yap-Wei*: Inference of nonlinear mixed effect models using Quasi-Monte Carlo methods.

Relevant workshops and courses participated in

June 2016 | *Attended a two day Drug Discovery and Development Project simulation workshop at NOVARTIS*: Worked in an interactive team tasked with the discovery and development of a new drug.

June 2017 | *4th GAMM Juniors summer school on "Bayesian Inference: probabilistic learning from data"*: A 3 day course on broad topics like Bayesian inference, probability theory and uncertainty quantification.

July 2020 | *Verified course on edX, MalariaX.*

Notable volunteering activities

2018-2019 | *Organized the first departmental meeting for 90-120 Ph.D. students*. I was a member of the core team of organizers who put together and conducted a two-day meeting for Ph.D. students in our institute. My tasks included designing the program and conducting workshops.

Lab and language skills

Wet-lab | *Basics of cloning in yeast (transformation, mini-prep), flow cytometry, and beginner in time-lapse (live cell) imaging*

Programming | *Intermediate in C++, R, MATLAB. Experienced user of MONOLIX.*